

What is claimed is:

1. A method for producing antibodies to a three-dimensional epitope of a bioactive human parathyroid hormone,
5 comprising:
 - a) immunizing an animal with the bioactive human parathyroid hormone; and
 - b) recovering antibodies from the animal;whereby the antibodies specifically recognize the three-
10 dimensional structure of the bioactive human parathyroid hormone.
2. The method of claim 1, further comprising immunizing the animal with the human parathyroid hormone a second time
15 before recovering the antibodies from the animal.
3. The method of claim 1, wherein the human parathyroid hormone is coupled to a carrier.
- 20 4. The method of claim 3, wherein the carrier is keyhole limpet hemocyanin.
5. The method of claim 1, wherein the bioactive human parathyroid hormone comprises SEQ ID NO: 1.
- 25 6. The method of claim 1 or 2, further comprising isolating the antibodies.
7. The method of claim 6, wherein the antibodies are isolated
30 by affinity chromatography.

8. The method of claim 7, wherein the antibodies are isolated by screening the antibodies with fragments of the human parathyroid hormone linked to a solid phase.

5 9. A method for producing antibodies that recognize and bind the bioactive, three-dimensional epitope of parathyroid hormone, comprising

a) immunizing an animal with parathyroid hormone;

10 b) immunizing the animal with parathyroid hormone a second time; and

c) recovering the antibodies from the animal, whereby the antibodies recognize and bind the bioactive, three-dimensional epitope of parathyroid hormone.

15 10. The method of claim 9, wherein the parathyroid hormone is conjugated to a carrier.

11. The method of claim 10, wherein the carrier is keyhole limpet hemocyanin.

20 12. The method of claim 9, wherein the parathyroid hormone is human parathyroid hormone.

25 13. The method of claim 9, further comprising isolating the antibodies so recovered.

14. The method of claim 13, wherein the antibodies are isolated by affinity chromatography.

30 15. The method of claim 14, wherein the antibodies are isolated by fragments of parathyroid hormone coupled to a solid phase.

16. The method of claim 15, wherein the fragments of parathyroid hormone are selected from the group consisting of amino acids 1-13, 13-34, and 39-84 of SEQ ID NO: 1.

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17. The method of claim 15, wherein the antibodies are isolated by a fragment of parathyroid hormone consisting of amino acids 1-13 of SEQ ID NO: 1.

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18. A method for producing antibodies that recognize and bind the bioactive, three-dimensional epitope of parathyroid hormone, comprising

a) immunizing an animal with parathyroid hormone, wherein the parathyroid hormone comprises amino acids 1-84 of SEQ ID NO: 1;

b) immunizing the animal with parathyroid hormone a second time; and

c) recovering the antibodies from the animal, whereby the antibodies recognize and bind the bioactive, three-dimensional epitope of parathyroid hormone.

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19. The method of claim 18, further comprising isolating the antibodies so recovered.

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20. The method of claim 18, wherein the bioactive three-dimensional epitope of parathyroid hormone consists of amino acids 1-13 of SEQ ID NO: 1.

21. A method for producing antibodies that recognize and bind the bioactive, three-dimensional amino terminus of parathyroid hormone, comprising
- a) immunizing an animal with parathyroid hormone conjugated to a keyhole limpet hemocyanin, wherein the parathyroid hormone comprises amino acids 1-84 of SEQ ID NO: 1;
 - b) subsequently immunizing the animal with parathyroid hormone; and
 - c) recovering the antibodies from the animal, whereby the antibodies recognize and bind the bioactive, three-dimensional amino terminus of parathyroid hormone.
22. The method of claim 21, wherein the bioactive three-dimensional amino terminus of parathyroid hormone consists of amino acids 1-13 of SEQ ID NO: 1.
23. An isolated antibody that recognizes and binds the bioactive, three-dimensional epitope of parathyroid hormone.
24. The isolated antibody of claim 23, wherein the bioactive, three dimensional epitope is the amino terminus of parathyroid hormone.
25. The isolated antibody of claim 23, wherein the parathyroid hormone is human parathyroid hormone.
26. The isolated antibody of claim 23, wherein the bioactive, three-dimensional epitope consists of amino acids 1-13 of SEQ ID NO: 1.

27. An isolated antibody recognizing a peptide comprising an amino acid sequence from Ser in the 1 position to Lys in the 13 position of SEQ ID NO: 1.

5 28. An isolated antibody according to claim 27 recognizing a peptide consisting of an amino acid sequence from Ser in the 1 position to Lys in the 13 position of SEQ ID NO: 1.

10 29. An antibody that is immunoreactive with the bioactive amino-terminal portion of human parathyroid hormone.

30. The antibody of claim 29, wherein the bioactive amino-terminal portion comprises amino acids 1-13 of SEQ ID NO: 1.

31. The antibody of claim 29, wherein the bioactive amino-terminal portion consists of amino acids 1-13 of SEQ ID NO: 1.

20 32. A therapeutic composition comprising the antibody of claim 29, and a pharmaceutically-acceptable carrier.

25 33. The antibody of claim 29, wherein the antibody reduces adenylate cyclase activity by binding to the bioactive portion of the parathyroid hormone.

34. Any one of the antibodies of claims 23-33, wherein the antibody is a polyclonal antibody.

30 35. Any one of the antibodies of claims 23-33, wherein the antibody is a monoclonal antibody.

36. Any one of the antibodies of claims 23-33, wherein the antibody is a humanized antibody.
37. Any one of the antibodies of claims 23-33, wherein the antibody is an antibody fragment.
38. Any one of the antibodies of claims 23-33 coupled to a detectable marker.
39. An antibody that specifically binds to the bioactive three-dimensional epitope of human parathyroid hormone, wherein the epitope consists of amino acids 1-13 of SEQ ID NO: 1.
40. A polyclonal antibody that recognizes and binds the bioactive three-dimensional epitope of human parathyroid hormone produced by a process comprising the following steps:
- a) immunizing an animal with human parathyroid hormone linked with keyhole limpet hemocyanin;
 - b) immunizing the animal with human parathyroid hormone; and
 - c) recovering the antibodies from the animal,
- whereby the antibodies recognize and bind the bioactive three-dimensional epitope of human parathyroid hormone.
41. A polyclonal antibody that recognizes and binds the bioactive three-dimensional epitope of human parathyroid hormone produced by a process comprising the following steps:
- a) immunizing an animal with human parathyroid hormone linked with keyhole limpet hemocyanin;

b) immunizing the animal with human parathyroid hormone;
and

c) recovering the antibodies from the animal,
whereby the antibodies recognize and bind the bioactive
5 three-dimensional epitope of human parathyroid hormone, and
wherein the bioactive three-dimensional epitope consists of
amino acids 1-13 of SEQ ID NO: 1.

42. An antibody selective for bioactive parathyroid hormone.

10 43. An antibody selective for bioactive parathyroid hormone,
wherein the antibody recognizes and binds at least one of
the first thirteen amino acids of SEQ ID NO: 1.

15 44. An isolated antibody that recognizes and binds the
bioactive, three-dimensional epitope of parathyroid
hormone, or a variant thereof.

20 45. An isolated antibody that recognizes and binds the
bioactive, three-dimensional epitope of parathyroid
hormone, or a fragment thereof.

25 46. A kit comprising an antibody that recognizes and binds the
bioactive, three-dimensional epitope of parathyroid
hormone.

47. The kit of claim 46, wherein the antibody is coupled with a
detectable label.

30 48. The kit of claim 46, wherein the bioactive, three-
dimensional epitope consists of amino acids 1-13 of SEQ ID
NO: 1.

49. The kit of claim 46, further comprising tools for obtaining a biological sample containing parathyroid hormone from a patient.

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50. The kit of claim 47, wherein the detectable label is selected from the group consisting of chemiluminescent markers, fluorescent markers, radioactive markers, and enzymatic markers.

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51. The kit of claim 47, wherein the detectable label is an acridinium ester.

52. A method for detecting bioactive parathyroid hormone in a sample, comprising

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a) exposing the sample to an antibody that recognizes and binds the bioactive three-dimensional epitope of parathyroid hormone; and

b) detecting the antibody-hormone complex,

thereby detecting the bioactive parathyroid hormone in the sample.

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53. The method of claim 52, wherein the antibody that recognizes and binds the bioactive three-dimensional epitope of parathyroid hormone is coupled with a detectable marker.

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54. The method of claim 52, further comprising exposing the antibody-hormone complex to another antibody that recognizes and binds parathyroid hormone before step (b).

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55. A method for detecting bioactive parathyroid hormone in a sample, comprising
- a) exposing the sample to a capture antibody that recognizes and binds the bioactive three-dimensional epitope of parathyroid hormone;
 - b) exposing the capture antibody-hormone complex to a detection antibody that binds a different epitope than the capture antibody; and
 - b) detecting the antibody-hormone complex,
- thereby detecting the bioactive parathyroid hormone in the sample.
56. The method of claim 55, wherein the detection antibody is coupled to a chemiluminescent marker.
57. The method of claim 56, wherein the chemiluminescent marker is an acridinium ester.
58. The method of claim 52 or 55, wherein the sample is from a patient with hyperparathyroidism.
59. The method of claim 52 or 55, wherein the sample is from a patient with hypoparathyroidism.
60. An immunoassay comprising an antibody that recognizes and binds the bioactive three-dimensional amino terminus of human parathyroid hormone.
61. The immunoassay of claim 60, wherein the bioactive three-dimensional amino terminus consists of amino acids 1-13 of
- SEQ ID NO: 1.